line 4. Support for new claims 83-86 can be found in the specification on page 7, lines 32-34. Support for new claim 87 can be found in the specification on page 8, lines 4-6 and lines 9-11

Telephone Conference

Applicants thank Examiner Basi for the helpful telephone conference of November 26, 2002, wherein the Office action and the pending claims were discussed with Applicants' representative.

Rejections Under 35 U.S.C. § 101

Claims 66-69 were rejected as not reciting that the polypeptides or polynucleotides were isolated or purified, thereby encompassing natural products. As discussed with Examiner Basi, Applicants have amended these claims to recite "isolated" thereby removing the rejection.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 12 and 55 are rejected for the use of the term" substantially." Applicants respectfully disagree that the term is indefinite, as the term is defined in the specification (see page 6, line 32 to page 7, line 1). However, solely to advance prosecution, and not for reasons pertaining to patentability, the claims are amended herein to recite "isolated."

Claim 61 was rejected as allegedly "high stringency" conditions are not disclosed. The Office action alleges that the claim is indefinite because the metes and bounds sequences depend upon the precise conditions under which hybridization is performed, including wash conditions. Applicants respectfully disagree with this rejection.

As noted in the specification, hybridization and washing are carried out using standard techniques (see page 8, line 4). There are many texts that teach standard stringent hybridization conditions, including Ausbel et al., *Current Protocols in Molecular Biology*, John Wiley & Sons (1989) (cited in the specification, see page 8, lines 5-6). Moreover, the specification lists specific exemplary low, moderate and high stringency conditions, including hybridization and wash conditions, on page 8, lines 4-15. For example, the specification describes several exemplary "high" stringency conditions as follows (see page 8, lines 4-6 and lines 9-11):

> "High stringency refers to DNA hybridization and wash conditions characterized by high temperature and low salt wash conditions, e.g. wash conditions of 65 °C at a salt concentration of at least 1 X SSC....For example, high stringency conditions include hybridization at about 42 °C and about 50% formamide, a first wash at 65 °C, about 2X SSC and 1% SDS; followed by a second wash at about 65 °C and about 0.1 X SSC."

Thus, the specification not only provides a citation of a reference text and the general characteristics of high stringency conditions, but also provides an exemplary set of conditions. One of skill in the art can readily utilize this information to identify hybridization and wash conditions of use, and thus can easily identify the sequences encompassed by the claim. Thus, the guidance provided by the specification is sufficient to provide one of skill in the art with a clear understanding of what constitutes high stringency conditions, and to determine the metes of the claimed sequences. Reconsideration and withdrawal of the rejection is respectfully required.

Claim 14 is rejected as allegedly not being in an appropriate format. Applicants respectfully disagree. Claim 14 includes a preamble: A method of identifying a candidate compound which inhibits estrogen receptor (ER)-dependent transcription comprising...". Claim 14 further includes two steps: (1) "contacting the compound with the AIB1 polypeptide of claim 12"; and (2) "determining whether the compound binds to the polypeptide." The claim also includes a conclusion that parallels the preamble to state that the preamble was achieved: "wherein binding of the compound to the polypeptide indicates that the compound inhibits ER-dependent transcription." For the convenience of the Examiner, and to clearly point out the components of the claim, claim 14 has been reiterated in the claim set shown above with appropriate formatting (carriage returns).

Applicants note that, in the claimed method, *transcription itself need not be measured*; it is solely the binding of the compound to the AIB1 polypeptide that indicates the polypeptide is of use. Thus, applicants submit that it would be inappropriate to include a step stating that transcription is measured in the body of this claim.

Claim 15, 16, 17, 19 and 20 are rejected for the recitation of a Pert/Arnt/Sim (PAS) domain, a bHLH domain or an ER-interacting domain. Claim 17 is canceled herein. Claims 15, 16, 19 are amended herein to recite "SEQ ID NO: 2,""SEQ ID NO: 3," or "SEQ ID NO: 8," as

appropriate. Applicants note that claims 19 and 20 were amended on June 4, 2001 to refer to an appropriate sequence identifier; this amendment is reflected in the list of claims provided herein.

Claim18 was rejected as allegedly it is unclear what is an "ER polypeptide" or "ER dependent transcription." In responding to this rejection, applicants have assumed that it is the abbreviation that renders the claim indefinite. As such, claim 18 is amended herein to recite "estrogen receptor." In addition, claim 18 has been amended to provide an appropriate conclusion. Applicants believe these amendments remove the rejection.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 12-20, 55-56, and 58-69 were rejected as allegedly not being described in the specification to convey that the inventors had possession of the subject matter at the time the application was filed. Applicants respectfully disagree with this assertion.

Applicants note that essential features of the claimed polynucleotides and polypeptides are described. For example, three domains are identified in SEQ ID NO: 4 that are relevant to the function of this polypeptide. Most notably, applicants have identified a sequence (the estrogen receptor interacting domain, SEQ ID NO: 8) responsible for interacting with the estrogen receptor (for example, see the specification at page 14, lines 14-15). Two additional domains, a basic helix-loop-helix (bHLH) and a pert/Arnt/Sim (PAS) domain are also identified. The PAS domain is noted to function as a protein interaction domain, mediating binding between AIB1 and other proteins (see the specification at page 14, lines 7-13). The bHLH domain is also described as participating in protein interactions (see the specification at page 14, lines 12-14). The specification describes that AIB1 polypeptides include polypeptides that contain domains that interact with a steroid hormone receptor, such as the estrogen receptor (e.g., see the specification at page 20, lines 34-35). A table of conservative substitutions is provided that clearly indicates what substitutions can be made to produce a mimetic. One of skill in the art, using the table provided, could clearly make substitutions outside of the estrogen receptor binding domain, that retain the function of the AIB1 polypeptide. Thus, a written description of a genus is clearly provided.

The Office action appears to indicate that "a recitation of structural features common to members of the genus" is required for appropriate written description, and that this structural feature is not described in the specification. Applicants respectfully disagree. As discussed

above, a *structural feature* is clearly described in the specification (the inclusion of estrogen receptor interacting domain, namely SEQ ID NO: 8). In addition, a *functional feature*, acting as a co-activator of estrogen receptors, is also fully described. Assays to determine if a peptide has the desired functional feature are also described (for example, see the specification at page 18, lines 18-26). Thus, applicants submit that the specification provides adequate written description for the claimed genus of polypeptides, for polynucleotides encoding these polypeptides, and for host cells and vectors including these polynucleotides.

Claims 12-20, 55-56 and 58-69 were rejected as allegedly not being enabled by the specification. Applicants respectfully disagree with this assertion.

The Office action notes that the specification is enabling for:

1. A purified polypeptide comprising SEQ ID NO: 4.
2. A purified nucleic acid comprising a sequence set forth as SEQ ID NO: 1.
3. Purified DNA molecules that are degenerate variants of SEQ ID NO: 1.
4. The complement of the nucleic acids described in (2) and (3) above.
5. Fragments of SEQ ID NO: 1 that are of sufficient length to serve as a hybridization probe.
6. Fragments of SEQ ID NO: 4 that are of use for producing antibodies.
7. Fragments of SEQ ID NO: 1 that binds the estrogen receptor.
8. Polypeptide fragments that bind the estrogen receptor that consist of SEQ ID NO: 4.
9. Vectors and host cells including polynucleotides encoding the polypeptides listed above; and
10. A process of identifying candidate compounds that inhibit estrogen receptor dependent transcription suing the polypeptides and polynucleotides listed above.

Applicants thank the Examiner for providing this helpful information.

However, the Office action alleges that the specification is not enabling for conservative variants, sequences identified by hybridization, or sequences that bind the steroid receptor. Applicants respectfully disagree with this rejection.

Claim 12 is directed to a polypeptide comprising SEQ ID NO: 8 that acts as a co-activator of the estrogen receptor. These polypeptides are described in the specification on page 7, lines 10-37. Applicants submit that the specification is fully enabling for conservative variants of SEQ ID NO: 4 that bind to an estrogen receptor, wherein the polypeptide includes SEQ ID NO: 8, as recited in claim 13 and dependent claims therefrom.

The Office action states that the instant fact pattern resembles that of *Ex parte Maizel*, 27 USPQ2d 1662 (BPAI 1992), wherein the full length sequence was disclosed, and a function of related sequences was disclosed. Applicants disagree with this comparison. Claim 1 of *Ex parte Maizel* is directed to "a DNA sequence which encodes a protein exhibiting a molecular weight between about 8 and about 14 kilodaltons upon gel exclusion chromotography, said protein having an amino acid sequence which includes the non-B-glactosidase derived sequence of amino acids displayed in Figure 4, *or a biologically functional equivalent thereof*..."

The Board noted that "biologically functional equivalent" could be related to proteins having conservative amino acid substitutions. However, the Board's finding was that the phrase "biologically functional equivalent thereof" encompassed "any proteins regardless of structure that is functionally equivalent to BCGF in terms of biological activity." The Board further concluded that based on the specification "DNAs encoding proteins having dissimilar structural configurations....would fall with the scope of the appellants' claims" and that the claims as written went beyond "proteins having amino acid substitutions wherein the substituted acids have similar hydrophyobicity and charge characteristics such that the substitutions are 'conservative'...." (see page 1665).

However, the present claims clearly recite a specific sequence (as compared to recitation of a molecular weight), recite that the substitutions are conservative, and recite that the proteins retain the polypeptide acts as a "co-activator of an estrogen receptor (as compared to a biologically equivalent function). Moreover, several structural elements (SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 8) have been identified that are important for this function. A table is provided in the specification on page 21 specifically listing conservative substitutions that can be made. A specific function of the polypeptide is recited in the claims, and specific assays to assess this function are described in the specification (e.g. see page 13, line 30 to page 14, line 2). Thus, applicants submit that the present specification, and the present pending claims are very different from the specification and claims described in *Ex parte Maizel*. Given the

guidance provided by the present specification (the sequences, identification of structural elements responsible for function, specific identification of a table of possible substitutions, and a complete description of a assay that can be used to identify sequences of use), claims to AIB1 polypeptides, and claims to nucleic acids encoding these AIB1polypeptides, are fully enabled by the specification. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants submit that the pending claims are now in condition for allowance, which action is requested. If any minor matters remain to be discussed before a Notice of Allowance is issued, the Examiner is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By _____
Susan Alpert Siegel, Ph.D.
Registration No. 43,121

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 226-7391
Facsimile: (503) 228-9446